SUBACUTE IMMUNE-MEDIATED POLYNEUROPATHY RESPONDING TO ORAL PREDNISONE DURING LONG-TERM VEMURAFENIB THERAPY.

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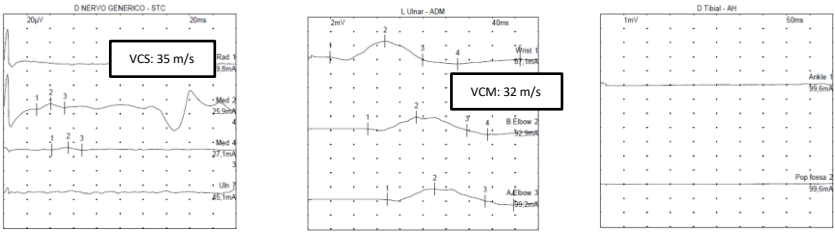
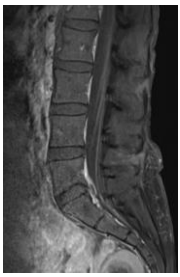
A 52-year-old woman with BRAF V600E–mutated metastatic melanoma, after ten years of treatment with vemurafenib-cobinetinib started complaining distal paraesthesia of the upper and lower limbs, with rapid clinical worsening: in few days she developed severe ascending weakness involving the four limbs, bilateral facial nerve palsy, with absent deep tendon reflexes, and urinary retention.



- **Nerve conduction studies**: sensory-motor polyneuropathy, primarily demyelinating with secondary axonal loss and active denervation.

- **Brain and total spine MRI**: cauda nerve roots thickening with gadolinium-enhancement.
- LCS analysis: markedly increased protein level (184 mg/dl), 28 cells/uL (mostly mononuclear cells).
- Microbiological, cytological analysis, and lymphocyte typing were normal.
- Extensive blood tests including anti-ganglioside and anti-paranodal antibodies, and onconeural antigens (tested both in LCS and serum) were negative.
- Total body CT scan excluded tumour progression.



Oncologic therapy was temporary discontinued and intravenous immunoglobulins (IVIg) 0.4 g/kg daily for 5 days were administered, with clinical stabilization. Prednisone 25 mg daily was started. The patient showed remarkable clinical improvement the following weeks (from wheelchair-bound to walking with unilateral support), with worsening at the attempt of stopping prednisone.

Monthly IVIg cycles led to only slight clinical improvement and early wearing-off, while intravenous methylprednisolone was not tolerated and poorly effective.

Prednisone 1 mg/kg was therefore started again with significant clinical improvement, that was maintained after dose decalage. At present, with a maintenance dose of prednisone 10 mg on alternate-day, she walks independently outdoors for long distances and does not complain limitations in hands function. She is still on oncologic therapy with vemurafenib-cobinetinib, with tumour control.

Vemurafenib is a BRAF inhibitor used for the treatment of BRAF V600E–mutated inoperable melanoma. BRAF inhibitors seem to increase immune cell recognition of melanoma cells by hyperactivated T-cell response, possibly leading to immune-mediated neuropathy through molecular mimicry with Schwann cells.

Few cases of immune-mediated polyneuropathy during vemurafenib therapy are described, with atypical features very similar to those in our patient: facial nerve involvement, poor response to IVIg, and good response to corticosteroids. All these cases developed polyneuropathy within few weeks after start of vemurafenib and were treated with vemurafenib discontinuance and oral prednisone.

Our findings suggest that immune-mediated subacute polyneuropathy might develop even years after starting vemurafenib; in this case antitumor therapy may be continued with concomitant low dose of corticosteroids.

References

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